late the composition and characteristics of the samples to their toxicity.

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P104-012
Workplace exposures equivalent to no or low observable adverse effect concentrations in animals: Step by step approach

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The particle size distribution of an aerosol is one of the main factors that determine the deposited fraction of inhaled particles in the various regions of the respiratory tract. The deposited, and subsequently retained, doses correlate closely with long-term toxic effects. Inhalation animal studies usually employ aerosols of small particle diameter and great homogeneity. By contrast, workers are usually exposed to coarser and more heterogenous aerosols. Yet, differences in deposited/retained doses between animals and humans due to particle size differences of aerosols have not been consistently taken into account in risk assessment (e.g., DNEL derivation under REACH). Here we describe an approach to calculate human exposures that are equivalent to the animal aerosol exposures for respiratory tract effects after inhalation, using workplace particle size information. Rat and workplace data for nickel sulfate and nickel oxide, used as examples, demonstrate that exposure levels used in the animal studies are equivalent to 4–11-fold higher levels of human workplace exposures. The described dosimetric approach is equally applicable to other metal and inorganic particulates that exert adverse effects on the respiratory tract after inhalation. This approach should be the first step in the derivation of an Occupational Exposure Limit based on animal local respiratory effects.

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Proteomic analysis of primary porcine bladder epithelial cells after BaP exposure

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Introduction: Epidemiological studies indicate an association between exposure to polycyclic aromatic hydrocarbons (key marker substance benzo[a]pyrene (BaP)) and bladder cancer development. The present study aims to identify differentially expressed proteins in primary porcine urinary epithelial cells (PUBEC) exposed to BaP. In this model the molecular phenotype is similar to that in human cells in vivo. Therefore this model seems to be quite suitable to monitor early proteomic changes following exposure to this carcinogen.

Methodology: PUBEC were isolated from bladders of freshly slaughtered pigs. After washing, cells derived from different bladders were pooled and resuspended in serum free culture medium (F-12 medium plus supplements). Cells cultured for 72 h were exposed to 0.5 μM BaP for another 24 h and finally lysed. The supernatant was separated by 2D Gel electrophoresis and proteins were visualised by colloidal coomassie and analysed with Delta 4.0 (Decodon) software. Further, spots of interest were excised from the gels and identified by MALDI-ToF mass spectrometry. The identification of the proteins was performed by searching MSDB and NCBInr protein databases with the special search tool Mascot.

Results: A total of 42 interesting proteins were differentially expressed and the interaction was analysed with protein network software. The results can be interpreted that BaP leads to an inhibition of the ubiquitin-proteosome pathway with subsequently stopped protein degradation. In consequence, several heat shock proteins and other molecular chaperones (valosin-containing protein or VCP) are up-regulated to handle the increase of misfolded and damaged proteins which are causing oxidative stress. The last is indicated by up-regulation of several cytoskeleton-associated proteins like beta-actin (ACTB) and keratin (KRT8, KRT2). In addition, mitochondrial-apoptosis regulatory protein (voltage-dependent anion channel (VDAC)) is up-regulated. In conclusion, the present study throws light into an early phase of cellular defense which is not unexpected regarding the low-dose and short-term exposure.

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Effects of peak concentrations on the neurotoxicity of styrene in workers

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The manufacture of fibreglass reinforced plastic products may give rise to substantial peak exposures to styrene. Such exposure pattern needs further consideration in terms of styrene neurotoxicity. The aim of this study was to verify if the neurotoxic effects of styrene are related to long-term peak exposures in workers at levels respecting the Quebec occupational exposure limits (8-h-TWA of 213 mg/m^3, 15-min average of 426 mg/m^3). A total of 104 workers (51 women, 53 men) were recruited in fibreglass-reinforced plastic industry in Quebec. Their average inhaled styrene concentration was used to separate them in three exposure categories: "Low" (<42.6 mg/m^3), "Medium" (42.6–<213 mg/m^3), and "High" (>213 mg/m^3). The exposed groups were then subdivided in two sub-groups: "with peaks" or "without peaks". Average styrene exposure was measured by personal passive dosimetry during the work shift on three consecutive days (Tuesday, Wednesday and Thursday). On one day, exposed workers were continuously monitored during the various tasks using a portable gas chromatograph taking samples every minute. The neurotoxicity of styrene was evaluated using a battery of internationally recognized sensory and neurophysiological tests. The results show that average 8-h TWA exposure in the visited industries ranged up to 520 mg/m^3. Important peak concentrations were identified and their average duration ranged between 12.5 and 22.1% of the work shift. In many cases, the peak concentrations largely exceeded the short-term limit value. Irritation of eyes, nose and throat was significantly more frequent in the High compared to the Medium or the Low-exposure groups. However, the different exposure scenarios involving average styrene exposure or peak exposures did not significantly alter the performance to any test. Several factors could have influenced our results: definition of peaks, statistical power or short exposure time.

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